

### **REMARKS**

In the Office Action, the Examiner stated that the claims were found to contain more than one invention and subjected the claims to a restriction requirement.

The Examiner asserts in the Office Action that the claims are distinct, each from the other, stating that the inventions are unrelated, being drawn to nucleic acids "that would have different nucleotide sequences, different modes of operation and different effects"; that they comprise divergent subject matter that have acquired a separate status in the art; that the distinct inventions require different searches but are not co-extensive; and that the examination of such distinct inventions would pose a serious burden on the Examiner.

Applicants respectfully disagree with the characterization that the inventions disclosed in the instant application require different searches and that their examination would pose a serious burden.

#### **The Claims Do Not Require Different Searches**

Applicants respectfully submit that the inventions have not acquired a separate status in the art, and that different searches are not required. Applicants respectfully submit that the inventions are related at least by structure, by functionality, and by utility.

All claims share common structural, functional, and utility elements, for at least the reason that all claims include at least a polynucleotide that encodes a non-oligomerizing tandem fluorescent protein (a polynucleotide of claim 88). These non-oligomerizing tandem fluorescent proteins share the common structural features of having a first monomer operatively linked to a second monomer, and further that the propensity of the tandem fluorescent protein to oligomerize is reduced or inhibited as compared to a monomer of the fluorescent protein. Applicants respectfully draw the Examiner's attention to the fact that this is true of the polynucleotides of all four of the inventions I-IV suggested by the Examiner. In addition, as is clear from the application, the polynucleotides of the invention encode fluorescent proteins related to naturally-occurring fluorescent proteins such as *Aequorea* GFP, *Discosoma* red fluorescent protein, and spectral variants thereof. The polynucleotides of the invention thus are seen to share common structural elements.

The polynucleotides of the invention also share common functions: they all encode proteins that fluoresce. The polynucleotides of the invention thus share the common mode of operation of providing fluorescent polypeptides; the common property of fluorescence similarly provides a common mode of operation for all the encoded polypeptides.

The polynucleotides of the invention further share common utility: they all encode proteins that are useful as sensors (e.g., pH indicators; see, for example, page 6, paragraph 18); as cell localization indicators (e.g., to indicate compartmentalization within a cell; see, for example, page 6, paragraph 20), as reporters of enzyme presence or activity (see, for example, page 7, paragraph 21); and as indicators of the presence of a molecule within a cell (e.g., see page 21, paragraph 22).

Applicants respectfully submit that the polynucleotides of the invention are recognized in the art as related subject matter, and do not comprise divergent subject matter that have acquired a separate status in the art. For example, a recent essay (Nature Biotechnology 20:28-29 (2002) "Negotiating the speed bumps to fluorescence", by Remington) discusses structural and functional similarities and common uses of different fluorescent proteins related to the ones encoded by the polynucleotides disclosed and claimed in the present application.

Thus, for at least the reasons that the polynucleotides of the invention are related by structure, function, and utility, applicants respectfully submit that claims 88-153 disclose related inventions. Applicants respectfully note that such commonality is clear even in the groupings of the restriction requirement itself: Inventions I and II bear the identical class and subclass classifications, and Inventions III and IV bear the identical class and subclass classifications.

#### **Searching the Claims Would Not Pose a Serious Burden**

Applicants respectfully disagree with the Examiner's statement that claims 88-153 would require different searches that are not co-extensive. As discussed above, the polynucleotides encode related fluorescent proteins sharing common elements and functions. The art recognizes such fluorescent proteins as related, and discusses such related proteins together (e.g., the review cited above). Accordingly, for at least the reasons that the claims recite related inventions, that the subject matter of the claims is treated as related in the scientific literature, and not as having acquired separate status in the art, Applicants respectfully submit that multiple searches are

unnecessary to identify references of relevance to all pending claims. A single search sufficing, no serious burden would be placed on the Examiner.

**Any Perceived Burden on the Examiner Can Be Reasonably Minimized by an Election of Species Requirement**

The pending claims include generic claims that recite polynucleotides encoding non-oligomerizing tandem fluorescent proteins that share common elements, functions and uses. The generic claims are suitably limited in scope, and define those fluorescent protein species that find use with the invention.

Applicants believe that additional restriction of the fluorescent protein species of Inventions I or II is inappropriate, and such proposed restriction would appear to be more consistent with election of species practice. If this restriction requirement were reassessed and made an election of species requirement, the Applicants would elect a single fluorescent species, and that species would be examined only in the event that the broader generic claims were held not to be allowable.

**Restriction Between Inventions I-IV and the further Restriction between Proteins Places a Serious Burden on the Applicant**

As discussed above, Applicants respectfully submit that the polynucleotides and the proteins they encode are related, sharing common structural, functional, and useful features despite having different sequences. For example, there are no fewer than 14 fluorescent polypeptide species recited in the claims. If the restrictions imposed by the Examiner were proper, Applicant would be required to file no fewer than 14 patent applications in order to protect polynucleotides encoding these polypeptides. Still more applications would be required to protect the methods of the invention. Applicants respectfully submit that such a large number of applications clearly presents an unreasonable financial burden in obtaining effective patent protection for the invention described in the present application.

As discussed previously in this case, it is unreasonable to assume that an applicant with limited financial resources would file so many applications. For at least this reason, this type of restriction requirement places some Applicants at a disadvantage in protecting their intellectual property. Thus, in the case where an applicant cannot afford the expense of numerous patent

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applications, the invention is essentially disclosed to the public in its entirety without proper compensation to the applicant in the form of patent protection for the invention.

### CONCLUSION

The Examiner is respectfully requested to reconsider the present restriction requirement in view of the arguments provided herein. Applicants respectfully request consideration of all claims.

**By provisionally electing with traverse, providing arguments herein, and requesting the Examiner to reconsider the restriction requirement, Applicants hereby preserve their right to Petition from the requirement for restriction under 37 C.F.R. § 1.144.**

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 08-1641.

Respectfully submitted,

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